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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/496,444	02/02/2000	Yumin Tao	1109	6243

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 03/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/496,444	TAO ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-18,22-25,27-53,64-66,70,71 and 75-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *22,65,70 and 75* is/are allowed.

6)☒ Claim(s) *2-18,23-25,27-53,64,66,71 and 76-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed November 17, 2003 has been entered.

Claims 1, 19-21, 26, 54-63, 67-69 and 72-74 are cancelled.

Claims 16, 18, 23-25, 27-33, 35-37, 39-53, 64, 66, 70-71 and 75 are currently amended.

Claims 76-81 are newly added.

Claims 2-18, 22-25, 27-53, 64-66, 70-71 and 75-81 are pending and are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

Claims 2-18, 23-25, 27-53, 64, 66 and 71 remain rejected, and newly added claims 76-81 are rejected, under 35 U.S.C. 112, first paragraph, for written description, for the reasons of record set forth in the office action mailed July 14, 2004.

Applicant's arguments filed November 17, 2003 have been fully considered but they are not persuasive.

Applicant argues that amended claim 64 requires the combination of function and structure sufficient to met the written description requirement, as the percent homology and activity of the isolated nucleic acid can be readily determined. Applicant additionally asserts that one of ordinary skill in the art could change the identity of SEQ ID NO:1 by up to 20% and screen the altered sequences for their ability to modulate the level of Cyclin E protein in a cell. Applicant also points out that the fact that the sequences have not been created does not prevent

them from being protected, as an invention may be complete and ready for patenting without having been reduced to practice. Further, in response to the Examiner's assertion that since a change in even a single nucleotide has the potential to alert the amino acid sequence of the encoded polypeptide, polynucleotides requiring 80% identity to SEQ ID NO:1 do read on widely variant species, Applicant disagrees and argues that only sequences having at least 80% identity to SEQ ID NO:1 and having the ability to modulate the level of Cyclin E fall within the scope of the claims. Applicant also asserts that silent and conservative variants can be readily obtained and characterized by one of skill in the art. (reply pages 13-14)

The rejection is maintained because the genus of claimed sequences in not adequately described. While amended claim 64 is directed to sequences that have at least 80% identity to the entire coding region of SEQ ID NO:1 and that modulate the level of Cyclin E protein in a cell, such sequences are not described in the specification, as the specification describes only a single nucleotide sequence of SEQ ID NO:1 obtained from maize that encodes a Cyclin E polypeptide. The specification does not describe a representative number of species falling within the scope of the claimed genus, nor the structural features unique to the genus. Furthermore, that one skilled in the art could make and screen sequences having at least have at least 80% identity to the entire coding region of SEQ ID NO:1 does not describe the structural features of SEQ ID NO:1 that are retained by functional variants. These arguments are applicable also to newly added claims 76-81, which encompass sequences having at least 85%, 90% or 95% identity to the entire coding region of SEQ ID NO:1

Additionally, while the Examiner does not dispute Applicant's assertion that sequences that have not been created may be patentable without having been reduced to practice, it is

maintained that such sequences must nonetheless be adequately described in order to be patentable.

The Examiner further maintains that merely asserting that only sequences having at least 80% identity (or at least 85%, 90% or 95% identity) to the entire coding region of SEQ ID NO:1to SEQ ID NO:1 and having the ability to modulate the level of Cyclin E fall within the scope of the claims does not describe the structure of such sequences. The claim limitation of "at least 80% identity" allows for the alteration of up to 327 base pairs of the 1636 base pairs of SEQ ID NO:1, yet the specification does not describe which 327 bases could be altered without affecting a sequence's ability to modulate the level of Cyclin E. Likewise, the claim limitations of at least 85%, 90% or 95% identity allow for the alteration of up to 245, 163 and 81 base pairs respectively of the 1636 base pairs of SEQ ID NO:1, yet the specification does not describe which 245, 163 or 81 bases could be altered without affecting a sequence's ability to modulate the level of Cyclin E.

Finally, the Examiner does not fully agree with Applicant's assertion that silent and conservative variants can be readily obtained and characterized by one of skill in the art. The Examiner does not dispute that one skilled in the art could readily obtain silent variants without the need to characterize the function of such variants, since the genetic code is universal and has long been established, and since silent variants would encode the same amino acid sequence as encoded by SEQ ID NO:1. However, the Examiner maintains that it is unclear whether one skilled in the art could readily obtain and characterize conservative variants, as conservative variants would encode an amino acid sequence different from that encoded by SEQ ID NO:1, and even a single conservative amino acid substitution in a protein could alter protein function.

In the instant case the specification does not describe or characterize even a one conservative amino acid substitution that would not affect the function of the polypeptide encoded by SEQ ID NO:1.

Claims 2-18, 23-25, 27-53, 64, 66 and 71 remain rejected, and newly added claims 76-81 are rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid of SEQ ID NO:1 or an isolated nucleic acid encoding SEQ ID NO:2, and complementary nucleotides thereof, does not reasonably provide enablement for polynucleotides having at least 80%, 85%, 90% or 95% identity to the entire coding region of SEQ ID NO:1, or for transgenic plants comprising said polynucleotides, or for methods of using said polynucleotides to achieve specific phenotypic effects in transgenic plant cells or plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the office action mailed July 14, 2004.

Applicant's arguments filed November 17, 2003 have been fully considered but they are not persuasive.

Applicant argues that undue experimentation would not be required to test sequences having less than 100% identity to SEQ ID NO:1, and points out that conserved regions required for Cyclin E protein activity are disclosed in the present specification, as well as methods for preparation and testing of the claimed nucleic acids. Applicant also points out that the limitations of the present claims focus on structural and functional features that are disclosed in the specification and that would be readily understood by those skilled in the art. In response to the

Examiner's assertion that the specification does not provide sufficient guidance for discriminating between operative and inoperative embodiments of sequence variants, Applicant points to Example 9 of the USPTO Written Description Guidelines as illustrative of the concept that one of ordinary skill in the art would know that screening for activity among hybridizing sequences would be required, since not all hybridizing sequences would be expected to have the activity of a reference sequence. Applicant points out that the specification specifically discloses how to make sequences having 80% identity to SEQ ID NO:1 and how to screen those sequences for function. (reply pages 15-17)

The Examiner maintains that undue experimentation would be required to practice the claimed invention. The undue experimentation lies in the process of selecting which variant sequences to test. Applicant provides no guidance with respect to discriminating between operative and nonoperative sequence embodiments before testing them for function, such that each and every sequence variant encompassed by the structural limitations of the claims would also have to be tested for functionality in order to determine whether or not it meets the functional limitations of the claims. Such trial and error testing of variant sequences constitutes undue experimentation, especially in light of the fact that only one functional sequence meeting the structural limitations is disclosed. With respect to the disclosure of conserved regions of Cyclin E, the Examiner maintains that the specification does not provide guidance with respect to which conserved regions, if any, are correlated with the recited function of modulating the level of Cyclin E. Additionally, the rejected claims do not require the presence of any such conserved region. Absent guidance with respect to which conserved regions, if any, are correlated with the recited function of modulating the level of Cyclin E, it would require undue

experimentation for one skilled in the art to determine which sequence variants to test for the recited function.

In response to the Examiner's observation that Cyclin E does not act independently and requires the presence of other proteins, Applicant observes that this is true of most proteins, and asserts that this does not make the effects of expressing Cyclin E any more or less unpredictable. Applicant argues that the regenerated plant will provide the machinery necessary for the isolated nucleic acid to function as predicted. Applicant further asserts that the Examiner has provided no evidence to controvert that the claimed isolated nucleic acid will function as predicted when expressed in a transgenic plant. (reply page 17)

The Examiner maintains that Cyclin E's specific requirement for and sensitivity to the presence of other particular proteins does make the effects of expressing Cyclin E unpredictable, because it is unpredictable when and where these proteins (Cyclin E's single catalytic partner CDK2, CDK inhibitory proteins, phosphorylases, and CyclinE/CDK2 substrates, for example) will be present in a quantity sufficient for an expressed Cyclin E sequence to exert a specific desired phenotypic effect. For example, an expressed Cyclin E sequence that increases the level of Cyclin E protein would not be able to exert an effect in the absence of Cyclin E's catalytic partner CDK2, or if CDK2 were present at a limiting concentration relative to endogenous Cyclin E. Even in the presence of a sufficient amount of CDK2, the ability of an expressed Cyclin E sequence that increases the level of Cyclin E protein to exert a specific phenotypic effect could additionally be affected by the availability of CyclinE/CDK2 substrates and/or the presence or absence of CDK inhibitory proteins and phosphorylases. Alternatively, an expressed

Cyclin E sequence that decreases the level of Cyclin E protein would not be able to exert an effect in the absence of endogenous Cyclin E expression, or might not be able to exert an effect in the presence of excess endogenous Cyclin E expression.

Additionally, while the Examiner does not dispute the general capacity of the regenerated plant to produce the proteins required for or that regulate Cyclin E function, the Examiner maintains that it is unpredictable whether expression of the isolated nucleic acid will produce the claimed phenotypic effects, because the claimed phenotypic effects require changing the level of Cyclin E in certain cell types and tissues at certain times or under certain conditions, and the specification does not provide sufficient guidance for one skilled in the art to determine, without undue experimentation, when, where and how to change the level of Cyclin E in order to achieve the desired phenotypic effects.

Furthermore, while it is not possible to provide direct evidence to controvert the assertion that the claimed isolated nucleic acid will function as predicted when expressed in a transgenic plant, since the prior art fails to teach the effect of expressing a Cyclin E sequence in transgenic plants, the teachings of the prior art as a whole suggest that the effects of expressing a Cyclin E sequence in any eukaryotic organism, including plants, would be unpredictable.

In response to the previous assertion by the Examiner that the claimed effects are unpredictable because the prior art teaches that the effect of overexpressing Cyclin E is unpredictable, Applicant points to the previously cited reference of Sgambato et al. as also teaching that the divergent effects of expressing their Cyclin E cDNA are not surprising, since there are other examples are known in which cell context influences the action of other genes

involved in growth control, and Applicant points further to pages 9-12 and 30 of the specification as disclosing that expression in different tissues and the use of different promoters would be required to obtain the claimed desired effects (reply pages 17-18).

With respect to the previously cited reference of Sgambato et al. as also teaching that the divergent effects of expressing their Cyclin E cDNA are not surprising, since there are other examples are known in which cell context influences the action of other genes involved in growth control, the Examiner maintains that such a teaching further underscores the unpredictability of expressing a Cyclin E sequence in a transgenic plant, as the teaching indicates that some form of guidance would be required with respect to when, where, how and how much to express a Cyclin E sequence in order to achieve a specific desired effect. With respect to Applicant's disclosure, the Examiner maintains that pages 9-12 and 30 do not disclose any specific combination of promoters and Cyclin E sequences which result in the any of the claimed phenotypic effects upon expression in a particular plant tissue.

Claims 27, 30, 46, 47 and 51 remain rejected, and claim 37, and claims 38 and 41 dependent thereon, are rejected, under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "alters" for the reasons of record set forth in the office action mailed July 14, 2004.

Applicant's arguments filed November 17, 2003 have been fully considered but they are not persuasive.

Applicant argues that the rejection should be withdrawn in light of the amendment of the claims (reply page 18).

The rejection is maintained because the amendment of the claims to recite a comparative basis does not fully address the previous rejection. It is still unclear in what way cell division, cell growth, organ growth the percent time of arrest, the amount of time in a cycle, and lag time are altered, as each of these characteristics may be altered in more than one way. The metes and bounds of "alters" are unclear.

Claim 42 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "embryogenic response" for the reasons of record set forth in the office action mailed July 14, 2004.

Applicant's arguments filed November 17, 2003 have been fully considered but they are not persuasive.

Applicant argues that the rejection should be withdrawn in light of the amendment of the claim (reply page 20).

The rejection is maintained because the amendment of claim 20 to recite that the embryos from the transformed plant have an increase in embryogenic response when compared to embryos from a control plant does not clarify what type of embryogenic response the claim encompasses, as embryogenesis may respond differentially to the presence or absence of a variety of factors, such as hormones, temperature, light, etc. The metes and bounds of "embryogenic response" are still unclear.

Claim Rejections - 35 USC § 101 and 35 USC § 112

Claim 18 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 18 is drawn to a seed comprising at least one nucleic acid of claim 64. Claim 18 as amended does not sufficiently distinguish over seed as they exist naturally, because the claim does not particularly point out any non-naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claim should be amended to indicate the hand of the inventor, e.g., by insertion of "transgenic", or "transformed", or other claim language that particularly indicates the hand of the inventor.

Claims 16-18 remain rejected under 35 U.S.C. 101 as not being supported by a specific and substantial utility, for the reasons of record set forth in the office action mailed September 20, 2002, for the reasons of record set forth in the office action mailed July 14, 2004.

Claims 16-18 also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention, for the reasons of record set forth in the office action mailed July 14, 2004.

Applicant's arguments filed March 25, 2003, have been fully considered but they are not persuasive.

Applicant argues that the rejection should be withdrawn since claims 23-53 present specific and substantial utilities for CycE nucleic acids, since the 1.132 Declaration filed June

28, 2001 provides evidence that the claimed sequence is a CycE nucleic acid, and since the Examiner has not provided evidence that the claimed nucleic acids will not function as predicted (reply page 21).

The Examiner maintains that Applicant's assertions are not germane to the instant rejection. The claims are not drawn to nucleic acids. Claims 16-17 are directed to a transgenic plant, including a corn plant, comprising at least one nucleic acid of claim 64. Claim 18 is drawn to a seed comprising at least one nucleic acid of claim 64. The Examiner maintains that there is no specific and substantial or well-established utility for plants transformed with the claimed nucleic acid molecules.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishida et al. (Nature Biotechnology, June 1996, Vol. 14, pages 745-750).

Claims 16-17 are directed to a transgenic plant, including a corn plant, comprising at least one nucleic acid of claim 64. Claim 18 is drawn to a seed comprising at least one nucleic acid of claim 64.

Ishida et al. teach transgenic corn plants, including their R1 progeny, transformed with an expression cassette comprising a GUS reporter gene and a Bar selectable marker gene (page 746

Figure 1; page 747 Figure 2page 749 Figure 5). The transgenic corn plants and progeny taught by Ishida et al. necessarily also comprise at least one nucleic acid of claim 64, as the specification indicates that the polynucleotide of SEQ ID NO:1 was obtained from corn (page 44 line 30).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Remarks

Claims 22, 65, 70 and 75 are allowed.

Claims 2-18, 23-25, 27-53, 64, 66, 71 and 76-81 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CC

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